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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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In re Application of:

Browning et al.

Application No.: 09/911,777 Group Art Unit: 1644

Filed: July 24, 2001 Examiner: Maher M. Haddad

For: BAFF, INHIBITORS THEREOF AND THEIR USE IN THE MODULATION OF B-CELL RESPONSE

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Michelle C. Small

Commissioner for Patents
Washington, DC 20231

Sir:

RESPONSE TO RESTRICTION REQUIREMENT

In an Office Action dated July 26, 2002, the Examiner required restriction under 35 U.S.C. § 121 between:

Group I - Claims 1-6 and 8-9, drawn to a method of stimulating B-cell growth, stimulating immunoglobulin production, co-stimulating B-cell growth and immunoglobulin production, and stimulating dendritic cell-induced B-cell growth and maturation in an animal comprising the step of administering a therapeutically effective amount of a BAFF land or an active fragment thereof, classified in Class 514, subclass 2

Group II - Claims 1-6 and 8-9, drawn to a method of stimulating B-cell growth, stimulating immunoglobulin production, co-stimulating B-cell growth and immunoglobulin production, and stimulating

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dendritic cell-induced B-cell growth and maturation in an animal comprising the step of administering a therapeutically effective amount of a BAFF ligand or an active fragment thereof and an anti-T antibody, classified in Class 424, subclass 140.1 and Class 514, subclass 2

Group III - Claims 1-6 and 8-9, drawn to a method of stimulating B-cell growth, stimulating immunoglobulin production, co-stimulating B-cell growth and immunoglobulin production, and stimulating dendritic cell-induced B-cell growth and maturation in an animal comprising the step of administering a therapeutically effective amount of a GAFF ligand or an active fragment thereof and a CD40 ligand, classified in Class 514, subclass 2

Group IV - Claims 1-9, drawn to a method of stimulating B-cell growth, stimulating immunoglobulin production, co-stimulating B-cell growth and immunoglobulin production, and stimulating dendritic cell-induced B-cell growth and maturation in an animal comprising the step of administering a therapeutically effective amount of a BAFF ligand or an active fragment thereof and an anti-CD40 ligand molecule, classified in Class 424, subclass 140.1; Class 514, subclass 2

Group V - Claims 10-16, drawn to a method of inhibiting B-cell growth, inhibiting immunoglobulin production, co-inhibiting B-cell growth and immunoglobulin production, and inhibiting dendritic cell-induced B-cell growth and maturation in an animal comprising the step of administering a therapeutically effective amount of an anti-BAFFA ligand molecule or an active fragment thereof, classified in Class 424, subclass 140.1

Group VI - Claims 10-15, drawn to a method of inhibiting B-cell growth, inhibiting immunoglobulin production, co-inhibiting B-cell growth and immunoglobulin production, and inhibiting dendritic cell-induced B-cell growth and maturation in an animal comprising the step of administering a therapeutically effective amount of a recombinant. inoperative BAFF ligand molecule or an active fragment thereof, classified in Class 514, subclass 2 and 424, subclass 140.1

Group VII - Claims 10-16, drawn to a method of inhibiting B-cell growth, inhibiting immunoglobulin production, co-inhibiting B-cell growth and immunoglobulin production, and inhibiting dendritic cell-induced B-cell growth and maturation in an animal comprising the step of administering a therapeutically effective

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amount of an antibody specific for BAFF ligand or an active fragment thereof, classified in Class 424, subclass 140.1

Group VIII - Claims 10-13, drawn to a method of inhibiting B-cell growth, inhibiting immunoglobulin production, co-inhibiting B-cell growth and immunoglobulin production, and inhibiting dendritic cell-induced B-cell growth and maturation in an animal comprising the step of administering a therapeutically effective amount of an antibody specific for BAFF ligand receptor or an epitope thereof, classified in Class 424, subclass 140.1; Class 514, subclass 2

Group IX - Claims 17 and 20-21, drawn to a method of treatment of an autoimmune disease comprising the step of administering a therapeutically effective amount of a BAFF ligand or an active fragment thereof, classified in Class 514, subclass 2

Group X - Claims 17 and 20-21, drawn to a method of treatment of an autoimmune disease comprising the step of administering a therapeutically effective amount of a BAFF ligand or an active fragment thereof and an anti-T antibody, classified in Class 514,subclass 2 and Class 424, subclass 140.1

Group XI - Claims 17, and 20-21, drawn to a method of treatment of an autoimmune disease comprising the step of administering a therapeutically effective amount of a BAFF ligand or an active fragment thereof and a CD40 ligand, classified in Class 514, subclass 2

Group XII - Claims 17 and 20-22, drawn to a method of treatment of an autoimmune disease comprising the step of administering a therapeutically effective amount of a BAFF ligand or an active fragment thereof and an anti CD40 ligand molecule, classified in Class 514, subclass 2 and Class 424, subclass 140.1

Group XIII - Claims 17 and 23-25, drawn to a method of treatment of an autoimmune disease comprising the step of administering a therapeutically effective amount of an anti-BAFF ligand molecule or an active fragment thereof, classified in Class 424, subclass 140.1

Group XIV - Claims 17 and 20-21, drawn to a method of treatment of an autoimmune disease comprising the step of administering a therapeutically effective amount of a recombinant, inoperative BAFF ligand molecule or an active fragment thereof, classified in Class 514, subclass 2

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Group XV - Claims 17 and 23-25, drawn to a method of treatment of an autoimmune disease comprising the step of administering a therapeutically effective amount of an antibody specific for BAFF ligand or an active fragment thereof, classified in Class 424, subclass 140.1

Group XVI - Claims 17 and 26, drawn to a method of treatment of an autoimmune disease comprising the step of administering a therapeutically effective amount of an antibody specific for BAFF ligand receptor or an epitope thereof, classified in Class 424, subclass 140.1

Group XVII - Claims 18-21, drawn to a method of treating a disorder related to BAFF-ligand comprising introducing into a desired cell a therapeutically effective amount of a vector containing a gene encoding for a BAFF-related molecule, and expressing said gene in said cell, wherein the BAFF-related molecule is a BAFF ligand or an active fragment thereof, classified in Class 514, subclass 44

Group XVIII - Claims 18-21, drawn to a method of treating a disorder related to BAFF-ligand comprising introducing into a desired cell a therapeutically effective amount of a vector containing a gene encoding for a BAFF-related molecule, and expressing said gene in said cell, wherein the BAFF-related molecule is a BAFF-ligand or an active fragment thereof and an anti-T antibody, classified in Class 514, subclass 44

Group XIX - Claims 18-21, drawn to a method of treating a disorder related to BAFF-ligand comprising introducing into a desired cell a therapeutically effective amount of a vector containing a gene encoding for a BAFF-related molecule, and expressing said gene in said cell, wherein the BAFF-related molecule is a BAFF-ligand or an active fragment thereof and a CD40 ligand, classified in Class 514, subclass 44

Group XX - Claims 18-22, drawn to a method of treating a disorder related to BAFF-ligand comprising introducing into a desired cell a therapeutically effective amount of a vector containing a gene encoding for a GAFF-related molecule and expressing said gene in said cell, wherein the BAFF-related molecule is a BAFF ligand or an active fragment thereof and an anti-CD40 ligand molecule classified in Class 514, subclass 44

Group XXI - Claims 18-19 and 23-25, drawn to a method of treating a disorder related to BAFF-ligand comprising introducing into a

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desired cell a therapeutically effective amount of a vector containing a gene encoding for a BAFF-related molecule, and expressing said gene in said cell, wherein the BAFF-related molecule is an anti-BAFF ligand molecule or an active fragment thereof, classified in Class 514, subclass 44

Group XXII - Claims 18-21, drawn to a method of treating a disorder related to BAFF-ligand comprising introducing into a desired cell a therapeutically effective amount of a vector containing a gene encoding for a BAFF-related molecule, and expressing said gene in said cell, wherein the BAFF-related molecule is a recombinant, inoperative BAFF ligand molecule or an active fragment thereof, classified in Class 514, subclass 44

Group XXIII - Claims 18-19 and 23-25, drawn to a method of treating a disorder related to BAFF-ligand comprising introducing into a desired cell a therapeutically effective amount of a vector containing a gene encoding for a BAFF-related molecule and expressing said gene in said cell, wherein the BAFF-related molecule is an antibody specific for BAFF-ligand or an active fragment thereof, classified in Class 514, subclass 44

Group XXIV - Claims 18-19 and 26, drawn to a method of treating a disorder related to BAFF-ligand comprising introducing into a desired cell a therapeutically effective amount of a vector containing a gene encoding for a BAFF-related molecule, and expressing said gene in said cell, wherein the BAFF-related molecule is an antibody specific for BAFF ligand receptor or an epitope thereof, classified in Class 514, subclass 44

Group XXV - Claim 27, drawn to a method of inducing a cell death comprising the administration of an went capable of interfering with the binding of a BAFF-ligand to a receptor, classified in Class 514, subclass 2, and Class 424, subclass 140.1

Group XXVI - Claims 28 and 32, drawn to a method of treating, suppressing or altering an immune response involving a signaling pathway between a BAFF-ligand and its receptor comprising the step of administering an effective amount of an agent capable of interfering with the association between the BAFF-ligand and its receptor, classified in Class 514, subclass 2, and Class 424, subclass 140.1

Group XXVII - Claim 29, drawn to a method of inhibiting inflammation comprising the step of administering a therapeutically effective

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amount of an antibody specific for a BAFF ligand or an active fragment thereof, classified in Class 424, subclass 140.1

Group XXVIII - Claim 30, drawn to a method of inhibiting inflammation comprising the step of administering a therapeutically effective amount of an antibody specific for a BAFF ligand receptor or epitope thereof, classified in Class 424, subclass 140.1

Group XXIX - Claim 31, drawn to a method of regulating hematopoietic cell development comprising the step of administering a therapeutically effective amount of a BAFF ligand or an active fragment thereof, classified in Class 514, subclass 2

Group XXX - Claims 33-37 and 39-40, drawn to method of treating hypertension in an animal comprising the step of administering a therapeutically effective amount of a B-cell growth inhibitor, wherein the B-cell growth inhibitor is an anti-BAFF ligand molecule or an active fragment thereof, classified in Class 424, subclass 140.1

Group XXXI - Claims 33-34 and 39-40, drawn to method of treating hypertension in an animal comprising the step of administering a therapeutically effective amount of a B-cell growth inhibitor, wherein the B-cell growth inhibitor is a recombinant, inoperative BAFF ligand molecule or an active fragment thereof, classified in Class 514, subclass 2

Group XXXII - Claims 33-37 and 39-40, drawn to method of treating hypertension in an animal comprising the step of administering a therapeutically effective amount of a B-cell growth inhibitor, wherein the B-cell growth inhibitor is an antibody specific for BAFF ligand or an active fragment thereof, classified in Class 424, subclass 140.1

Group XXXIII - Claims 33-34 and 38-40, drawn to method of treating hypertension in an animal comprising the step of administering a therapeutically effective amount of a B-cell growth inhibitor, wherein the B-cell growth inhibitor is an antibody specific for BAFF ligand receptor or an epitope thereof, classified in Class 424, subclass 140.1

Group XXXIV - Claim 41-43, drawn to method of treating cardiovascular disorders in an animal comprising the step of administering a therapeutically effective an anti-BAFF ligand molecule or an active fragment thereof, classified in Class 424, subclass 140.1

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Group XXXV - Claim 41-43, drawn to method of treating cardiovascular disorders in an animal comprising the step of administering a therapeutically effective a recombinant, inoperative BAFF ligand molecule or an active fragment thereof, classified in Class 424, subclass 140.1, and Class 514, subclass 2

Group XXXVI - Claim 41-43, drawn to method of treating cardiovascular disorders in an animal comprising the step of administering a therapeutically effective an antibody specific for BAFF ligand or an active fragment thereof, classified in Class 424, subclass 140.1

Group XXXVII - Claim 41-43, drawn to method of treating cardiovascular disorders in an animal comprising the step of administering a therapeutically effective an antibody specific for BAFF ligand receptor or an epitope thereof, classified in Class 424, subclass 140.1

Group XXXVIII - Claims 44-45, drawn to method of treating renal disorders in an animal comprising the step of administering a therapeutically effective amount of an anti-BAFF ligand molecule or an active fragment thereof, classified in Class 424, subclass 140.1 and Class 514, subclass 2

Group XXXIX - Claims 44-45, drawn to method of treating renal disorders in an animal comprising the step of administering a therapeutically effective amount of a recombinant inoperative BAFF-ligand molecule or an active fragment thereof, classified in Class 424, subclass 140.1, and Class 514, subclass 2

Group XL - Claims 44-45, drawn to method of treating renal disorders in an animal comprising the step of administering a therapeutically effective amount of an antibody specific for BAFF-ligand or an active fragment thereof, classified in Class 424, subclass 140.1

Group XLI - Claims 44-45, drawn to method of treating renal disorders in an animal comprising the step of administering a therapeutically effective amount of an antibody specific for BAFF-ligand receptor or an epitope thereof, classified in Class 424, subclass 140.1.

Group XLII - Claim 46, drawn to a method of treating B-cell lympho-proliferate disorders comprising the step of administering a therapeutically effective amount of an anti-BAFF ligand molecule or an active fragment thereof, classified in Class 424, subclass 140.1

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Group XLIII - Claim 46, drawn to a method of treating B-cell lympho-proliferate disorders comprising the step of administering a therapeutically effective amount of a recombinant inoperative BAFF-ligand molecule or an active fragment thereof, classified in Class 424, subclass 140.1, and Class 514, subclass 2

Group XLIV - Claim 46, drawn to a method of treating B-cell lympho-proliferate disorders comprising the step of administering a therapeutically effective amount of an antibody specific for BAFF-ligand or an active fragment thereof, classified in Class 424, subclass 140.1

Group XLV - Claim 46, drawn to a method of treating B-cell lympho-proliferate disorders comprising the step of administering a therapeutically effective amount of an antibody specific for BAFF-ligand receptor or an epitope thereof, classified in Class 424, subclass 140.1

Group XLVI - Claims 47-50, drawn to a method of treating B-cell production in the treatment of immunosuppressive diseases comprising the step of administering a BAFF-ligand or an active fragment thereof, classified in Class 514, subclass 2

Group XLVII - Claims 47-50, drawn to a method of treating B-cell production in the treatment of immunosuppressive diseases comprising the step of administering a BAFF-ligand or an active fragment thereof and an anti-T antibody, classified in Class 514, subclass 2, and Class 424, subclass 140.1

Group XLVIII - Claims 47-50, drawn to a method of treating B-cell production in the treatment of immunosuppressive diseases comprising the step of administering a BAFF-ligand or an active fragment thereof and a CD40 ligand, classified in Class 514, subclass 2 and Class 424, subclass 140.1

Group XLIX - Claims 47-50, drawn to a method of treating B-cell production in the treatment of immunosuppressive diseases comprising the step of administering a BAFF-ligand or an active fragment thereof and an anti-CD40 ligand molecule, classified in Class 514, subclass 2 and Class 424, subclass 140.1

Group L - Claims 47-50, drawn to a method of treating B-cell production in the treatment of immunosuppressive diseases comprising the step of administering an anti-BAFF-ligand molecule or an active fragment thereof, classified in Class 424, subclass 140.1

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Group LI - Claims 47-50, drawn to a method of treating B-cell production in the treatment of immunosuppressive diseases comprising the step of administering a recombinant, inoperative BAFF-ligand molecule or an active fragment thereof, classified in Class 514, subclass 2

Group LII - Claims 47-50, drawn to a method of treating B-cell production in the treatment of immunosuppressive diseases comprising the step of administering an antibody specific for BAFF-ligand or an active fragment thereof, classified in Class 424, subclass 140.1

Group LIII - Claims 47, 49-50, drawn to a method of treating B-cell production in the treatment of immunosuppressive diseases comprising the step of administering an antibody specific for BAFF-ligand receptor or an epitope thereof, classified in Class 514, subclass 2 and Class 424, subclass 140.1

Applicants provisionally elect with traverse to prosecute group VII (claims 10-16). Applicants respectfully submit that the 53-way restriction requirement imposed by the Examiner is improper for the reasons recited below and should be withdrawn.

Applicants note that groups V, VII, XIII, XV-XXVIII, XXX, XXXII - XXXIV, XXXVI -XXXVIII, XL - XLII, XLIV, XLV, L, and LII (claims 10-17, 23-26, 29, 30, 33-40, and 33-50) are designated by the Examiner as classified in class 424, subclass 140.1. Additionally, groups II, IV, VI - VIII, X, XII, XXV, XXVI, XXXV, XXXIX, XLIII, XLVII - XLIX, and LIII (claims 1-9, 10-17, 20-22, 27, 28, 32, and 41-50) are also designated by the Examiner as having at least some subject matter classified in the same class and subclass (class 424, subclass 140.1). Thus, at least claims 1-17, 20-30, and 32-50 have substantially overlapping fields of search as indicated by the classification.

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For a restriction requirement to be proper, a showing of serious burden on the Examiner is required. A serious burden may be *prima facie* shown by separate classification, separate status in the art, or a different field of search. *See* Manual of Patent Examining Procedure (MPEP) §§ 802-803. When inventions are classified in the same class and subclass, MPEP § 802.02 requires the Examiner to show different fields of search, e.g., that it is necessary to search for one of the distinct subjects in places where no pertinent art to the other subject exists. The present restriction requirement provides no such showing. The Examiner merely alleges that a different field of search would be required based upon the structurally distinct products recited and the various methods of use comprising distinct steps. The Examiner does not explain what structural differences in the "products" or "steps" would necessitate a field of search where no pertinent art to the other subject exists. Thus, the Examiner has failed to make a *prima facie* showing that such a different field of search exists.

While recognizing the policy underlying the restriction practice, Applicants note that the present 53-way restriction requirement is excessive and cost-prohibitive. Therefore, Applicants request the Examiner to withdraw the restriction requirement and consider issuing a revised restriction with a possible election of species that is more appropriate in the present case. In particular, Applicants request the Examiner to consider regrouping the claims as follows:

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Proposed Group I

Claims 10-17, 20-31, and 33-45, drawn to methods of to methods of inhibiting, co-inhibiting, or suppressing immune response, B-cell growth and/or maturation and/or immunoglobulin production B-cell growth, methods of inducing cell death, and methods of treating/inhibiting an autoimmune disease, inflammation, hypertension, cardiovascular, renal and/or B-cell lympho-proliferative disorders.

Proposed Group II

Claims 1-9 and 47-50, drawn to methods of stimulating B-cell growth/immunoglobulin production/dendritic cell-induced B-cell growth and maturation/inducting cell death/immune response.

Proposed Group III (Linking Group)

Claims 18, 19, 28, 31, and 32, drawn to methods of treating, suppressing or altering an immune response, a disorder related to BAFF ligand, and methods regulating hematopoietic cell development.

Within each proposed group, Applicants believe that a search could be carried out without under burden to the Examiner. However, if the Examiner believes that a species election is further required for the purposes of focusing the initial search, Applicants propose species election within each group as follows: (a) a BAFF ligand or an active fragment thereof; (b) a BAFF ligand or an active fragment thereof and an anti-T antibody; (c) a BAFF ligand or an active fragment thereof and a CD40 ligand; (d) a BAFF ligand or an active fragment thereof and an anti-CD40 ligand molecule; (e) a anti-BAFF ligand molecule or an

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active fragment thereof; (f) a recombinant, inoperative BAFF ligand molecule or an active fragment thereof; (g) an antibody specific for BAFF ligand or an active fragment thereof; and (h) an antibody specific for BAFF ligand receptor or an epitope thereof.

Applicants further believe that the various disorders recited in the claims can be searched without undue burden to the Examiner. However, should be the Examiner believe that a further election of species is necessary, Applicants propose the following species subgroups: (i) autoimmune disease; (ii) inflammation; (iii) renal disorders; (iv) hypertension; (v) cardiovascular disorders; (vi) B-cell limpho-proliferative disorders; and (vii) immunosuppresive disease.

Should the Examiner agree with the Applicants' proposed revision to the restriction requirement, Applicants provisionally elect the claims of proposed group I. If the Examiner believes species election is necessary, Applicants provisionally elect the species of group (g) and subgroup (i). Applicants invite the Examiner to contact their representative, Leslie A. McDonell, at (617) 452-1650 if any additional clarification would be helpful.

A petition for a five-month extension of time is attached with this response.

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Please charge an extension of time fee in the amount of $1,960.00 as required by 37 C.F.R. § 1.17 to deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON,
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Dated: Dec 20, 2002

By: Leslie McDonell
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